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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,117	LI ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 135-138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 135-138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, and 135-138 are pending and examined on the merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/14/2007 has been entered.

This Office Action is in reply to Applicants' correspondence of 02/14/2006. Claim(s) 3-134 is/are cancelled; no claim(s) is/are withdrawn; claim(s) 135-138 has/have been newly added; claim(s) 1 has/have been amended.

Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put this application in condition for allowance. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is **NON-FINAL**.

Priority

This instant application claims priority to provisional applications 60/427,202 (filed 11/19/2002) and 60/434,434 (filed 12-19-2002). However, the subject matter of the examined claims (claims 1-3, methods using SPHK1 gene copy number) was not disclosed in the '202 provisional application, thus the claims do not have priority to the

'202 provisional application. The subject matter of the examined claims is disclosed in the '434 provisional application, thus the claims have priority to the 60/434,434 provisional application (filed 12-19-2002).

Claim Rejections - 35 USC § 112 1st¶ - Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 135-138 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> screening methods comprising determining sphingosine kinase 1 (SPHK1) gene copy number, wherein said sphingosine kinase 1 (SPHK1) gene encodes an mRNA comprising SEQ ID NO: 3, in a test sample, and comparing the test sample copy number to data for a control gene copy number obtained from a control sample of the same tissue type as the test sample,

does not reasonably provide enablement for method comprising analysis of the broadly claimed 'sphingosine kinase 1 (SPHK1) gene copy number' and comparison to a control gene copy number from any 'corresponding tissue'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the invention and breadth of the claims

The claims of the instant application are drawn to methods for screening for a cancer comprising determining SPHK1 gene copy number, and as such encompass

determining the copy number of any 'sphingosine kinase 1 (SPHK1) gene'.

Claim 1 encompasses a comparison of a gene copy number to any control gene copy number from any 'corresponding tissue'.

The nature of the claims requires knowledge of a correlation between copy number of the broadly claimed 'sphingosine kinase 1 (SPHK1) gene' and the suggestion of the presence of a precancerous lesion or a cancer.

Direction provided by the specification and working example

The specification of the instant application asserts that it has been determined that SPHK1 is amplified and/or overexpressed in human cancers (p.66). The specification asserts that human chromosome region 17q25 is one of the most frequently amplified regions in human cancer, and that in the process of characterizing a 17q25.2 amplicon SPHK1 was found amplified in several tumor samples (p.67). The specification teaches that amplification of SPHK1 was determined by microarray analysis (p.67).

The specification teaches several definitions relevant to the breadth of the rejected claims. The specification teaches that 'cancer' includes the presence of cells possessing characteristics typical of cancer-causing cells, and specifically includes leukemic cells. The specification further defines a 'gene' as a region on genome capable of being transcribed to an RNA that has a regulatory or catalytic function or encodes a protein and encompasses spice variants, allelic variants, and transcripts arising from alternative promoter or poly-adenylation sites (p.32). The specification further defines SPHK1 as encompassing polymorphic variants, alleles, mutants, and

interspecies homologs with various, not clearly defined, levels of homology and identity to GenBank NM_021972 (nucleic acid sequence), Genbank NP_069907.2 (polypeptide sequence), and SEQ ID NO: 1, 2, and 3 (nucleic acid and polypeptide sequences). (p.66).

Because the claimed method comprises determining gene amplification, it is relevant to point out that the instant specification broadly defines the term 'amplification' as encompassing amplification, duplication, and multiplication, of a gene yielding about 3.0 fold or more copies. However, an SPHK1 gene copy number of less than 3.0 fold can still be considered an amplification (p.34). The specification further defines an 'amplicon' as the amplification product of a gene, indicating that the term includes partially amplified SPHK1 (p.35).

Thus given the definitions provided by the specification, the claimed methods encompass detecting amplification of any portion of a gene sequence with even a small degree of sequence similarity to the any variant of an SPHK1 gene or cDNA sequence (where it is noted that the provided SEQ ID NO: 1 and 2 are cDNA sequences, and not genomic sequences that encode the SPHK1 transcript). For example, a polymorphic variant of an SPHK1 gene which contains a three nucleotide repeat insertion would be a gene amplification.

The specification provides an example of the analysis of SPHK1 gene amplification in cells from human tumors (Examples I, II, and III, pages 111-114). The Examples of the specification teach that DNA microarray based CGH was used to survey the genome for gene amplification, and it was determined that SPHK1 is

frequently amplified in tumor tissues and cell lines. The specification teaches analysis of SPHK1 gene copy number in breast, ovarian, colon, bladder, and lung tumors (Table 1). The specification teaches that SPHK1 gene amplification was detected from 3% to 33% of the time. For example, amplification was detected in 1 out of 30 lung tumor samples. In the case of bladder cancer, amplification was found in 3 out of 9 samples (33%).

The reporting of '-fold amplification' is not clear within the specification (p.34), as the specification does not clearly set forth what is considered a '-fold amplification'. For example, assuming that a non-cancer sample has two copies of a gene (diploid), would detection of three copies of the gene in a tumor sample be considered a 1.5-fold amplification (2 x 1.5 = 3), or considered a 1-fold amplification (there is 1 more copy of the gene), or considered a 3-fold amplification (there are 3 copies of the gene), or some other -fold amplification. Is fold amplification reported relative to a non-cancer sample, or an absolute number of copies of the gene in a sample.

The specification does not provide the sequence of the microarray probes used to determined SPHK1 gene amplification, nor the method in which gene amplification was determined for the data in Table 1, nor the nature of the amplicon (e.g. the portion of the SPHK1 gene that is amplified in a tumor sample).

State of the art, level of skill in the art, and level of unpredictability

While the state of the art and level of skill in the art with regard to the detection and quantitation of a particular nucleic acid sequence in a sample is high, the level of unpredictability in associating any particular gene or copy number of a gene with a

phenotype is even higher, where in the instant case the unpredictability is intensified by the breadth of the claims with regard to the SPHK1 gene and control copy number from any 'corresponding tissue'. The level of unpredictability is demonstrated by the prior art, the post filing art, and the instant specification.

Though the prior art teaches a role of sphingosine kinase in the development of cancer phenotypes (Xia et al, 2000, as cited in the IDS), the prior art does not teach the reliable association of amplification of any SPHK1 gene as broadly claimed and defined in the instant specification with the suggestion of cancer.

Additionally, post-filing art reveals that most gene association studies are typically wrong. Lucentini (2004) teaches that it is strikingly common for follow-up studies to find gene-disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in the gene association studies (middle column, 1st complete paragraph). It is thus not established by the teachings provided in the instant specification whether or not a measure of copy number of any SPHK1 gene, as broadly defined in the specification, can reliably suggest the presence of cancer.

And while the specification teaches the breadth of the term 'SPHK1 gene', the examples presented in the specification do not address the different sequences encompassed by the claims. For example while the claims encompass analysis of any

polymorphic variant, the specification does not teach the analysis of any variants of the SPHK1 gene. The art teaches a variety of polymorphisms in the SPHK1 gene including at least 27 SNPs (GeneCard for protein-coding SPHK1, pages 7-8). Notably, one SNP (rs3744040; CAG to TAG) creates a Gln to STOP codon change in the protein-coding region. Based on the prior art of Xia et al (which teaches a role of over expression of the sphingosine kinase in cancer development) coupled with the teachings of the instant application (which asserts that gene amplification leads to overexpression (Table 2)), it is unpredictable as to whether or not amplification of a gene containing, for example, the rs3744040 SNP (coding for a truncated amino acid sequence), or any other SNP, would be indicative of cancer.

Additionally, post-filing art reveals that most gene association studies are typically wrong. Lucentini (2004) teaches that it is strikingly common for follow-up studies to find gene-disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in the gene association studies (middle column, 1st complete paragraph). It is thus not established by the teachings provided in the instant specification whether or not a measure of copy number of any SPHK1 gene, as broadly defined in the specification, can reliably suggest the presence of cancer.

Quantity of experimentation required

A large amount of experimentation would have to be performed in order to make and use the claimed invention. Such experimentation would include examining any possible variant of the SPHK1 gene as broadly defined in the specification to determine which of the possible myriad of sequences are suitable for screening for the cancers recited in the claims. Application of the method to the specifically recited forms of cancer would require validation every possible gene variant to establish that such 'SPHK1 gene' copy number suggests the presence of cancer'. Such experimentation would involve the analysis of an enormous number of nucleic acid sequences.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the lack of guidance by the applicant and the lack of working examples, it is the conclusion that an undue amount of experimentation would be required to make and use the claimed invention.

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 112 1st¶ as lacking enablement. Applicants' remarks indicate that the amendments to claim 1 moot the Examiner's bases for the rejection of the claims (p. 5 of remarks of 02/14/2007). The amendments to the claims have been fully considered but are not found to be sufficient to put the claims in condition for allowance.

Initially it is noted that the presently pending claims are drawn to a method for screening, where a detectable amplification suggests the presence of a cancer. As such the data presented in the instant specification, combined with the general teachings of the prior art, support the notion that the amplification of the SPHK1 gene is suggestive of the presence of cancer. Previous claims were drawn to a method for diagnosing, where the specification (p.31) defines 'diagnosing a cancer' as determining the presence or absence of a cancer or precancerous condition in an animal, where the data presented in the instant specification is not considered to be robust with regard to the required definitive association.

However, the claims still encompass the analysis of the copy number of the 'sphingosine kinase 1 (SPHK1) gene', where the breadth of the nucleic acid sequences encompassed by the term, as defined in the specification (p.66), essentially renders the term meaningless with regard to any sequence limitation. Further the specification provides only the sequences of the SPHK1 mRNA/cDNA (SEQ ID NO: 1) and the protein-coding portion thereof (SEQ ID NO: 3), and does not provide for any particular nucleic acid sequence (disclosed as a SEQ ID NO) that is suitable for providing any sequence considered an SPHK1 gene. And while the examples of the specification indicate particular methods used to analyze SPHK1 gene amplification (i.e. microarray based CGH, p.111) as well as other general methods for copy number analysis (p.73-76), the specification does not provide any particular structures (i.e. sequences of primers or probes) used in the analysis of SPHK1 gene copy number. Thus given the lack of any structural limitations within the claim, and the breadth of the term 'SPHK1' as

defined by the specification, the copy number detection encompassed by the claim makes the claim of such a scope as to be not fully enabled.

Further with regard to claim 1, which requires comparison of a test copy number to 'a control gene copy number obtained from a corresponding tissue', the limitation of 'a corresponding tissue' does not serve to limit the actual control gene copy number that is used in a comparison. As such the claim may encompass the detection of any gene copy number in a test sample, where the claim may be limited to an enabled breadth if the recited 'a corresponding tissue' is amended to specify 'a control sample of the same tissue type as the test sample', where the specification (p.42) defines 'control sample' as a sample obtained from a cancer-free population.

This rejection as set forth is MAINTAINED.

Claim Rejections - 35 USC § 112 1st – Written Description

Claims 1, 2, and 135-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

> Applicant is referred to the guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5, page 1099-111 (also available at www.uspto.gov).

The rejected claims are broadly drawn to methods for diagnosing cancer comprising determining SPHK1 gene copy number. The rejected claims provide no structural limitation regarding what is encompassed by the term 'sphingosine kinase 1

(SPHK1) gene'.

When the claims are analyzed in light of the specification, the instant invention encompasses methods comprising the analysis of an enormous and wide variety of nucleic acid sequences. The claims are broadly drawn to screening for cancer by determining SPHK1 gene copy number in a test sample. The specification teaches a broad definition of 'gene' as a region on the genome that is capable of being transcribed to an RNA (p.32), and encompasses all SPHK1 transcripts that may be found including splice variants, allelic variants, and transcripts that occur because of alternative promoter sites or alternative poly-adenylation sites (p.33). The specification further teaches a broad definition of 'SPHK1', indicating that the term 'SPHK1' may include polymorphic variants, alleles, mutants, and interspecies homologs that have (i) for example as little as 60% nucleotide identity to GenBank NM_021972, (ii) as little as 65% amino acid homology to GenBank NP_068807.2, (iii) for example as little as 60% homology with the nucleotide sequence of SEQ ID NO: 1, or (iv) 'substantial sequence homology with the encoded amino acid (for example, SEQ ID NO: 2)' with no clear definition of 'substantial sequence homology' (p.66). Additionally, the specification teaches a definition of 'amplicon' as an amplification product that may include a part of SPHK1 (p.35). Thus the rejected claims encompass analysis of any portion of any variant of any SPHK1 gene, which may include gene sequences very different from the disclosed SEQ ID NO: 1, and genes that encode polypeptides very different from the disclosed SEQ ID NO: 2, including sequences containing any polymorphisms (e.g. any

insertion, deletion, or repeat at any location within the gene) and mutations not taught by the instant specification and not yet known in the art.

In analyzing whether the written description requirement is met for genus claims for genus claims, it is first determined whether a representative number of species have been described by their complete structure. Nucleic acids of such a large genus as encompassed by the rejected claims have not been taught by the specification. The specification of the instant application discloses only SEQ ID NO: 1 (a human SPHK1 cDNA sequence), SEQ ID NO: 3 (the protein coding portion of SEQ ID NO: 1), and SEQ ID NO: 2 (the amino acid sequence encoded by SEQ ID NO: 3).

In analyzing whether the written description requirement is met for genus claims for genus claims it is next determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence, gene name, and specific polymorphic position), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the specification provides only the sequence of the human SPHK1 gene (SEQ ID NO: 1 and 3) and the encoded amino acid sequence (SEQ ID NO: 2). The specification does not provide any characteristics that would allow one to identify any other genes from another organism or any particular portions or fragments or variants of the disclosed sequence that would allow for the diagnosis of cancer based on amplification of the non-disclosed gene.

> Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:
>
> > It appears to be well settled that a single species can rarely, if ever, afford

> sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the instant application, with the exception of a method for diagnosing cancer comprising determining the copy number of a gene consisting of the particular sequences disclosed in the specification, one of skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides (i.e. any SPHK1 genes the amplification of which is suggestive of cancer), regardless of the complexity or simplicity of the method of identification. Adequate written description requires more than a mere statement that any genetic variants or fragment of the gene is part of the claimed invention and a qualitative description of the nature of the variant (e.g. amplification is associated with cancer).

In conclusion, the limited information provided regarding the association of SPHK1 (including disclosure only of SEQ ID NO: 1, 2, and 3) gene amplification with cancer is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of methods comprising the analysis of any gene variants or fragments besides those particularly disclosed in the specification at the time the application was filed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 112 1st¶ as lacking adequate written description of the claimed subject matter. Applicants' remarks indicate that the amendments to claim 1 moot the Examiner's bases for the rejection of the claims (p. 5 of remarks of 02/14/2007). The amendments to the claims have been fully considered but are not found to be sufficient to put the claims in condition for allowance.

The amendments to the claims do not serve limit the claimed subject matter to within the scope of the subject matter described in the instant specification. The claims still encompass the analysis of the copy number of the 'sphingosine kinase 1 (SPHK1) gene', where the breadth of the nucleic acid sequences encompassed by the term, as defined in the specification (p.66), essentially renders the term meaningless with regard to any sequence limitation.

Applicants may circumvent the rejection of claims for lack of written description by inclusion of claim language introducing the structural limitations of the sequences taught in the instant specification into the claims, e.g.: 'wherein said sphingosine kinase 1 (SPHK1) gene encodes an mRNA comprising SEQ ID NO: 3'.

The rejection as set forth is MAINTAINED.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Suehiro et al (2000).

Suehiro et al teaches the comparative genomic hybridization analysis of ovarian carcinoma cells.

Regarding claim 1, the reference teaches CGH analysis of DNA extracted from ovarian clear cell carcinomas using trimmed tumor samples (p.51 – Tumor material; CGH). The reference specifically teaches the analysis of copy number of the chromosomal region 17q25-qter, a region which encompasses the human SPHK1 gene. Thus the analysis of tumor DNA by CGH is determining SPHK1 gene copy number in a sample from a region suspected to be cancerous and generating data for a test gene copy number (p.51 – Microscopy and digital image analysis), relevant to part (a) of claim 1. Relevant to part (b), the reference also teaches the CGH analysis of normal DNA (p.51 –CGH), and the simultaneous analysis of labeled DNA (from tumor and normal tissue) by hybridization to normal metaphase spreads, which is a corresponding tissue. Thus the analysis results in a comparison of test and control gene copy numbers. The reference further teaches that amplification of the 17q25-qter region (which contains the SPHK1 gene) indicates the presence of cancer (p.53 correlations between clinical stages and CNAs; Table 4; Table 5).

Regarding claim 2, the reference teaches the use of normal DNA as a control, and hybridization to normal metaphase spreads (p.51 – CGH). Thus the comparison to

the control is a comparison to a normal diploid sample in which the copy number of the 17q25-qter region is two copies per cell.

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 102 as anticipated by Suehiro et al. Applicant argues (Remarks pages 4-5) that Suehiro et al does not expressly or inherently teach determining SPHK1 gene copy number or that amplification of an SPHK1 gene in a test sample relative to a control indicates the presence of a precancerous lesion or cancer in a mammal. This argument has been fully and carefully considered but is not found to be persuasive.

Applicants have presented the argument (p.4 of Remarks) that the claims of the instant specification are drawn to a ***species*** of invention requiring the analysis of the SPHK1 gene copy number, whereas the cited prior art is a ***genus*** where a larger genomic portion (i.e. 17q25-qter) is analyzed and that larger portion contains the required SPHK1 gene. While Applicants argument that many gene are contained within the 17q25-qter region, and Suehiro et al does not mention the SPHK1 gene at all, is accurate, the methods of Suehiro comprising analysis of the 17q25-qter region inherently encompasses the required SPHK1 gene. The application of the Suehiro et al reference to the rejected claims is more accurately described as an issue of 'comprising' language as opposed to an issue of genus versus species. In the instant case the claims are drawn to methods 'comprising' (i.e. open to the inclusion of additional, unrecited elements or method steps (see MPEP 2111.03)), where an analysis of the

amplification of the 17q25-qter region is a method comprising the analysis of the copy number of a sphingosine kinase (SPHK1) gene.

In the instant case, applicants may circumvent the rejection based on the cited prior art of Suehiro et al by amending the claims such that the claimed method requires analysis only of the SPHK1 gene. Alternatively, Applicants may circumvent the rejection based on the cited prior art of Suehiro et al by removing the recited element of ovarian cancer from the listing of cancers for which the claimed method is a screen.

The rejection as set forth is MAINTAINED.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Stephen Kapushoc
Art Unit 1634

BJ FORMAN, PH.D.
PRIMARY EXAMINER